REMARKS/ARGUMENTS

Status of the Claims

Claims 1-33 were pending. In the instant Response, Applicants have amended claims 1, 8, and 33; added new claims 33-51; and cancelled claims 2-7 and 9-23, without prejudice. Therefore, with the entry of the present amendments, claims 1, 8, 33-51 are currently pending in the application.

Support for the amendments can be found in the application in general. In particular, support for claims directed to reducing caloric efficiency can be found at least at page 23, example 7, of the specification. Support for claims directed to reducing non-high fat food or both high fat and low fat food intake or appetite, can be found at least at, page 16, example 1, where standard chow was fed to the animals; and page 22, example 6, to page 24, example 8, where high fat and low fat chow were fed to the animals. Support for claims directed to reducing nutrient availability can be found at least at page 5, lines 15-17. Support for claims directed to PYY agonists having a higher affinity for the Y2 receptor over the Y1 receptor and/or Y5 over Y1 can be found at least at page 2, lines 12-14; Table 1 of pages 10 and 11; and page 29, lines 9-16. Support for claims directed to amounts of PYY or PYY agonists of about 1 μg to 5 mg per day in single or divided doses can be found at least at page 7, lines 17-19; amounts of about 5 μg to 100 μg per day in a single or divided doses can be found at least at page 14, line 14; and amounts of about 0.1 μg/kg to 10 μg/kg per day in a single or divided dose can be found at least at page 14, lines 14-15, where it is taught that a preferred amount is about 5 μg to about 500 μg/day for a 50 kg patient (*i.e,* 0.1 μg/kg to 10 μg/kg per day). Support for the additional step of administering a GLP-1, an exendin, an amylin, their agonists or any combination thereof, can be found at least at page 7, line 23 to page 8, line 4. Applicants submit that no new matter has been introduced into the currently pending claims.

Applicants note with appreciation that on page 2 of the Office Action, the Examiner has withdrawn the rejection of claims 6, 7, 11, 12, 31, and 32 under 35 U.S.C. 103(a) for allegedly being unpatentable over Malaisse-Lagae *et al.* (*Experientia* **33**:915-917, 1997) (hereinafter

"Malaisse-Lagae") in view of Yoshinaga *et al.* (*Am. J. Physiol.* **263**:G695-701, 1992) (hereinafter "Yoshinaga"), Allen *et al.* (*Digestion* **30**:225-262, 1984), and Ueno *et al.* (*Gastroenterology* **117**:1427-1432, 1999) (hereinafter "Ueno"). In the instant Response, Applicants have further amended these claims (or canceled them). Applicants submit that the amended claims remain patentable over the art of record.

Issues under 35 U.S.C. 112, 1st paragraph

Claims 6, 7, 11, 12, 31, and 32 are rejected under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the written description requirement. The Patent Office alleges that claims 6, 7, 11, 12, 31, and 32 introduce new matter because the specific dosages recited in the claims are not supported by the specification. While not conceding the Patent Office's contention that there is no support for the claimed ranges, Applicants have amended the claims to recite the broader range originally presented. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. 112, first paragraph.

Issues under 35 U.S.C. 103(a)

Claims 1, 4, 5, 8-10, 23, 29, and 33 remain rejected under 35 U.S.C. 103(a) for allegedly being unpatentable over Malaisse-Lagae in view of Yoshinaga, Allen, and Ueno. Applicants respectfully traverse this rejection as applied to the claims as previously pending and to the extent it may apply to the claims as currently amended. Applicants respectfully reserve the right to prosecute any subject matter not included in the scope of the instantly amended claims.

The Patent Office, at page 4, last paragraph, of the Office Action, cites Malaisse-Lagae as teaching that pancreatic polypeptide (PP) reduces food intake and suppresses body weight gain in hyperphagic obese mice, and Ueno as teaching decreased food intake and body weight in pancreatic polypeptide-overexpressing mice and the inhibitory effect of PP on the pancreatic exocrine secretion. Therefore, the Patent Office concludes that one of skill in the art would be convinced that the inhibitory effect of PP on pancreatic exocrine secretion is linked to reduced food intake and suppression of body weight gain. Applicants, however, cannot find any such

suggestion of the link between pancreatic exocrine secretion and reduced food intake and suppression of body weight gain in the cited references. In the paragraph referred to by the Patent Office, Ueno states that "PP can stimulate (or, at high doses, inhibit) gastric secretion, inhibit pancreatic secretion, decrease gallbladder contraction, and modify gastric and upper intestinal motilities." Also, Ueno states that "PP appears to have some metabolic effects . . . [and that PP, at physiological doses, has been shown to] inhibit pancreatic exocrine secretion and relax the gallbladder. Ueno, however, does not suggest a link between pancreatic exocrine secretion and reduced food intake and suppression of body weight gain.

The Patent Office then cites Yoshinaga as teaching that PYY is structurally similar to PP and that PYY is a potent inhibitor of pancreatic exocrine, gastric acid, and insulin secretion. Therefore, the Patent Office concludes on page 5, first paragraph of the Office Action, that it would have been obvious to one having ordinary skill in the art at the time the invention was made to substitute PP for PYY in the method of treating obesity as taught by Malaisse-Lagae with a reasonable expectation of success. Applicants disagree with the Patent Office's conclusion for at least two reasons. The first reason relates to the previous paragraph where it is shown that no connection has been made to link inhibition of pancreatic exocrine secretion to reduced food intake and suppression of body weight gain. Because one of skill in the art could not have reasonably assumed that inhibition of pancreatic exocrine secretion was useful to reduce food intake and suppress weight gain, the teachings of Yoshinaga, that PYY is an inhibitor of pancreatic exocrine secretion, would not render PYY's use in reducing food intake or suppressing body weight gain in hyperphagic obese mice obvious. In other words, there is no teaching or suggestion in the cited references that PYY could reduce food intake or suppress body weight gain.

The second reason that the references, alone or in combination, do not render the claimed invention obvious is that the Patent Office appears to be utilizing a new measure of obviousness in reasoning that because PYY is structurally related to PP and may have a function in common with PP, then it would have been obvious to have used PYY in place of PP for any purpose where PP has been used. However, the Patent Office has also cited the Allen reference which

teaches that while PYY and NPY are structurally related (and while they may share some similar functions, for example, when administered centrally they stimulated food intake, Iyengar *et al. J Pharmacol Exp Ther* **289:** 1031-40, 1999), they are not equivalent in all functions. In other words, based on the known art, the use of one would not have rendered obvious the use of the other.

Applicants, in the instant Response, have submitted a supplemental Information Disclosure Statement and Form PTO-1449 citing Morley *et al.* (*Live Sciences* **41:**2157-2165, 1987) (hereinafter "Morley") and Morley (*Neuropsychobiology* **21:**22-30, 1989). Applicants submit that one of skill in the art, based on his or her own experience and knowledge of the prior art at the time the application was filed, would have found the Morley reference to be a non-enabling disclosure. To cite only one example why this is a non-enabling disclosure, in order to demonstrate the proposition that peripheral administration of PYY caused weight loss, Morley conducted experiments utilizing 12-week-old mice that were administered with sulfated cholecystokinin (CCK-8S), bombesin and PYY. The results are provided at page 2161, last paragraph before the discussion, and Figures 3A, 3B, 4A, 4B, 5A, and 5B.

Morley concludes that neither CCK-8S nor bombesin caused significant weight loss or altered food intake. The skilled artisan, in looking at Figures 3A and B, would note that the mice given saline, the controls, gained over 1 gram of weight during the course of the experiment. The mice given CCK-8S or bombesin appeared to have gained less than half a gram. In contrast, in Figure 5A, the skilled artisan would note that the mice given PYY lost a little over 1 gram of weight. However, the skilled artisan would also note that for that particular set of experiments only, the mice given saline, the controls, did not gain weight. In other words, in all the other experiments measuring weight change, see, Figures 1A-1D and Figures 3A-3B, the control mice given saline gained weight. Thus, the expected response of the control mice is to gain weight. In this experiment with PYY, however, the mice given saline did not gain weight. Therefore, the controls did not work as expected for this experiment, indicating that something may have failed in the experiment, there was an error in the reported results or both. Given the nature of the

error, the skilled artisan would be loath to reach the same conclusion as Morley, that it showed that PYY has an effect on weight loss.

The literature, at the time of the invention, would not have provided much assistance to the skilled artisan in believing Morley's conclusion as there were studies that PYY was ineffective in reducing food intake, Garlick *et al.* (*Amer Physiol Soc* 1990) and Gomez *et al.* (*Amer Physiol Soc* 1995) attached, was a potent orexigenic agent when administered centrally, Morley *et al.* (*Brain Research* **341**:200-3, 1985), and that PYY and PYY agonists could be used to increase weight gain (U.S. Patent No. 5,912,227).

CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance and requests that a timely Notice of Allowance be issued in this case. The Examiner is encouraged to call the undersigned attorney to discuss any issues related to the prosecution of the instant application.

Applicants believe that no fee is necessitated by the present paper. However, in the event any fees are due or any amount is to be credited, Applicants authorize the Commissioner of Patents to debit or credit Deposit Account No. 010535.

Respectfully submitted,

Mi K. Kim
Reg. No. 44,830

9/22/2003

AMYLIN PHARMACEUTICALS, INC.
9360 Towne Centre Drive
San Diego, CA 92121
Phone: (858) 552-2200
Facsimile: (858) 552-1936